Serial change in $^{123}$I-MIBG myocardial scintigraphy in non-insulin-dependent diabetes mellitus

Shigeki Nagamachi,* Seishi Jinouchi,* Takeshi Kurose,** Ryuichi Nishi,* Keiichi Kawai,*** Shigemi Futami,* Shozo Tamura* and Shigeru Matsukura**

*Department of Radiology, **Third Department of Internal Medicine, and ***Central Research Laboratories, Miyazaki Medical College

**ORIGINAL ARTICLE**

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**INTRODUCTION**

Along with cardiac denervation, cardiac autonomic neuropathy is a significant prognostic factor for diabetes mellitus.1-3 Many studies have reported the usefulness of...
$^{123}$I-MIBG (MIBG) scintigraphy in monitoring diabetic cardiac sympathetic nerve dysfunction. Decreases in MIBG uptake have been reported to correlate with the body mass index (BMI), systolic blood pressure, disturbed left ventricular diastolic filling, and QT interval length. Diabetic patients with autonomic neuropathy (AN) have a considerably decreased MIBG uptake when compared to diabetics without AN, but few studies have been performed to clarify whether a disturbed cardiac sympathetic nervous system can recover in diabetic patients. In insulin-dependent diabetes mellitus (IDDM), poor glycemic control constitutes an essential determinant in the progression of MIBG uptake, whereas the impact of glycemic control on the serial change in MIBG uptake has not been determined in non-insulin-dependent diabetes mellitus (NIDDM). Although a few limited studies with aldose reductase inhibitor have been reported, the results have not been generally accepted.

The current study was undertaken to clarify how myocardial MIBG distribution changes in a clinical follow-up of patients with NIDDM and to find the determinant factor influencing the changes in MIBG distribution. At the same time, the serial changes in the coefficient variance of the R-R interval of rest ECG (CVR-R), nerve conducting velocity of the posterior tibial nerve (NCV), and MIBG uptake were evaluated.

**MATERIALS AND METHODS**

Twenty patients, all over 43 years of age and diagnosed with NIDDM by the criteria of the National Diabetes Group, were enrolled in this study. All subjects had a low probability of coronary artery disease based on the absence of cardiovascular symptoms, a normal resting ECG, a normal maximal exercise ECG, and a normal stress $^{201}$Tl-chloride myocardial SPECT. Based on echocardiographic analysis, no subjects had evidence of left ventricular hypertrophy, and all had normal left ventricular function. All subjects agreed to participate in the study and signed an informed consent form approved by the Institutional Review Board of Miyazaki Medical College.

To block tracer uptake in the thyroid gland, each subject received 10 mg of potassium iodine 2 days before the investigation and 10 mg daily for 1 or 2 days afterwards. Patients remained on their normal diets and drug regimens except for drugs that could cause changes in sympathetic activity. Anterior planar images were obtained 15 minutes (early) and 4 hours (delayed) after $^{123}$I-MIBG (111 MBq) injection by means of a rotating gamma camera (ZLC7500, Shimadzu) equipped with a Krypton collimator. Energy discrimination was provided by a 20% window centered on the 159 keV photopeak of $^{123}$I.

For the semiquantitative analysis, the heart-to-uppermediastinum uptake ratio (H/M) was calculated by the conventional ROI method on both early and delayed planar images, as previously reported. After correction for the physical decay of $^{123}$I, the tracer washout rate from the myocardium (WR) was calculated by the following formula:

$$WR = \frac{\text{early} ([H] - [M]) - \text{delayed} ([H] - [M])}{\text{early} ([H] - [M])} \times 100\%$$

According to the serial change in H/M, we divided all patients into two groups: those whose H/M values were higher in the follow-up study than in the baseline study were placed in the improved group. The patients whose H/M values were lower in the follow-up study than in the baseline study were placed in the unimproved group. Because H/M is affected by the size of the heart, the cardiac chamber size was confirmed by $^{201}$Tl-SPECT to be unchanged between the baseline and the follow-up study.

The clinical characteristics, the mean laboratory data values and MIBG parameters in the baseline study for the two groups were compared (Table 1). All values are shown as the mean ± SD. In each group, means for each parameter in the baseline study data and the follow-up study data were compared (Table 2). Scheffe’s F-test for multiple comparisons was applied to detect the statistically significant difference as defined by ANOVA. A comparison of serial data within one group was performed by means of Wilcoxon’s matched-pairs signed-rank test. A value of $p < 0.05$ was considered statistically significant.

Non-parametric testing (Fisher’s exact test) was also employed to evaluate whether the serial changes in MIBG parameters were independent of the change in other

**Fig. 1** A 58-year-old patient with NIDDM for 13 years. In the first study (upper row), myocardial MIBG uptake was not noted on either the early (left) or delayed image (right). H/M was 1.7 on the early and 1.8 on the delayed image. WR was 11.8%. In the follow-up study 2 years later (lower row), normal myocardial uptake was noted on both the early (left) and delayed images (right). H/M increased to 3.2 on the early and 3.1 on the delayed image. WR decreased to 3.1%.